

File B2
Mark up claim
wherein the small multilamellar vesicles comprise:

(a) a lipid component comprising 20-30 mol % of an ionizable amino lipid, a steric barrier lipid and additional lipid components selected from among neutral lipids and sterols; and

(b) [ODNs] oligodeoxynucleotides contained in the lumen or interlamellar spaces of the small multilamellar vesicles.

REMARKS

This is in response to the Official Action mailed April 23, 2002 for the above-captioned application. Applicants request a three month extension of time, and enclose the appropriate fee. The Commissioner is authorized to charge any additional fees or credit any overpayments to Deposit Account No. 15-0610.

Reconsideration and further examination of the application in view of the remarks herein are respectfully requested.

Claims 1-9 are examined in this application.

The Examiner objected to the specification, stating that the term DOPE was not defined. Applicants have amended the specification to insert the art-recognized meaning of this abbreviation, dioleoylphosphatidylethanolamine. This definition is shown in the Wheeler reference, on Page 16, lines 4-5.

The Examiner rejected claims 1-9 under 35 USC § 112, second paragraph. Claim 1 has been amended to replace the abbreviation ODN with the term "oligodeoxynucleotides." The Examiner also object to the term "lumen or interlamellar spaces" as lacking antecedent basis. Rejections for lack of antecedent basis are not appropriate as a mere formalism, and should only be made when there is actual ambiguity resulting from the language. MPEP § 2173.05. Applicants respectfully point out that the existence of a lumen or interlamellar spaces in a lipid small multilamellar vesicle is inherent, in much the same way that a circle inherently has a circumference. Thus, formalistic recitation of the terms to say that the small multilamellar vesicle has a lumen or interlamellar spaces in not necessary, and would only serve to introduce unnecessary verbiage to the claims. Similarly, the rejection of the claims because of the use of abbreviations is formalistic, and not based on any actual ambiguity. The abbreviations employed

are common in the art (since the chemical names are such mouthfuls) and are defined in the specification. Thus, the Examiner has not made it clear why a person skilled in the art would have any trouble understanding the scope of the claims when read as a person skilled in the art, and in light of the specification.

The Examiner also objected to the term "steric barrier lipid," but did not say why this term was indefinite. The Examiner bears the burden in the first instance of explaining why a person skilled in the art could not determine the scope of the claims. *In re Cordova*, 10 U.S.P.Q. 2d 1949, 1952 (POBAI 1989). As would be apparent to a person skilled in the art having read the specification, a "steric barrier lipid" is a lipid which provides a structural (or steric) barrier that physically blocks molecular interactions. Thus, as explained on Page 11 of the application,

Suitable steric barrier lipids include PEG-lipids such as PEG-CerC₁₄ and PEG-CerC₂₀. Other examples of steric barrier lipids which can be used include polyamide oligomer lipids (PAO-lipids) and gangliosides.

Thus, Applicants respectfully traverse this rejection.

On the merits, the Examiner rejected claims 1-9 under 35 USC § 103 as obvious over Wheeler (WO 96/40964). In arguing the relationship of Wheeler to the present claims, the Examiner has characterized Wheeler as disclosing a cationic amino lipid as part of a lipid particle. It appears that the Examiner is equating Wheeler's cationic lipid with the ionizable amino lipid of claim 1. Wheeler, however, does not disclose an ionizable amino lipid because the amino lipids disclosed therein are all permanent cations.

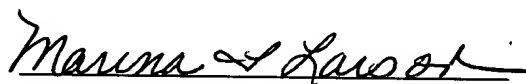
Assuming single bonds, the nitrogen in an amino group can have either three substituent groups, or four. When there are four groups attached to the nitrogen, the nitrogen atom has a positive charge. Such amines are termed "quaternary amines." When there are only three groups, the nitrogen atom is charge neutral, but can become positively charged in solutions of low pH by picking up a hydrogen ion (H⁺). This latter process is reversible as a function of pH. Thus, the amino lipids of this type are ionizable. The Examiner's arguments do not deal with this distinction, and thus fail to show that the invention as claimed is obvious. Applicants would further point out that compositions made using Wheeler's quaternary amino lipids can not be charge neutralized by changing the pH. This means that excess oligonucleotides which are complexed to the exterior of a lipid particle (which can be deleterious) can not be conveniently

removed by simply changing the pH. For the foregoing reasons, Applicants submit that claims 1-9 are not obvious over Wheeler.

The Examiner has also rejected the claims for obviousness-type double patenting over the claims of issued US Patent No. 6,287,591. Applicants will submit a terminal disclaimer, if appropriate, after a determination has been made that the claims are otherwise allowable.

For these reasons, and in view of the above amendments and subject to the submission of a terminal disclaimer, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,

A handwritten signature in cursive script, appearing to read "Marina T. Larson", is written over a horizontal line.

Marina T. Larson, Ph.D.
Attorney/Agent for Applicant(s)
Reg. No. 32038

970 468 6600